IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	
Shinichi YASUEDA et al.	:	Docket No. 2000_0436A
Serial No. 09/529,882	:	Group Art Unit 1615
Filed April 21, 2000	:	Examiner C. Evans

AQUEOUS LIQUID PHARMACEUTICAL COMPOSITION

#6
Withdrawn
6/29/01

RESPONSE

Assistant Commissioner for Patents,
Washington, D.C.

Sir:

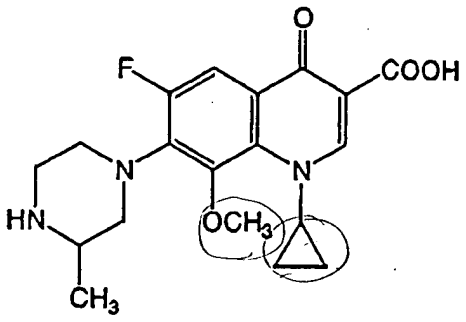
Responsive to the Office Action of March 26, 2001, Applicants submit the following remarks in support of the patentability of the present invention over the disclosure of the reference relied upon by the Examiner in rejecting the claims. Further and favorable reconsideration is respectfully requested in view of these remarks.

Thus, the rejection of claims 1-11 under 35 U.S.C. § 103(a) as being unpatentable over Ogata et al. is respectfully traversed.

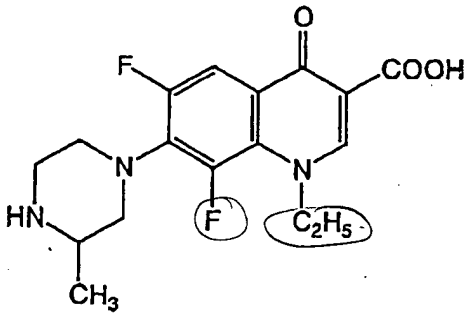
The present invention provides an aqueous liquid pharmaceutical composition comprising Gatifloxacin or its salt and disodium edetate (claims 1-5 and 9-11). The present invention also provides a method for raising corneal permeability of Gatifloxacin comprising incorporating disodium edetate into eye drops containing Gatifloxacin or its salt (claim 6); a method for preventing precipitation of Gatifloxacin crystals comprising incorporating disodium edetate into an aqueous liquid preparation containing Gatifloxacin or its salt (claim 7); and a method for preventing coloration of Gatifloxacin comprising incorporating disodium edetate into an aqueous liquid preparation containing Gatifloxacin or its salt (claim 8).

As noted in the first paragraph in column 1 of Ogata et al., the reference "relates to a stable isotonic aqueous solution of a specific quinolone carboxylic acid biocide or a salt thereof" (emphasis added), more particularly the compound 1-ethyl-6,8-difluoro-1,4-dihydro-7-(3-methyl-1-piperazinyl)-4-oxoquinoline-3-carboxylic acid.

As acknowledged by the Examiner, there is no disclosure about Gatifloxacin in the Ogata et al. reference. As seen from the following chemical structures, Gatifloxacin is completely different from the synthetic antimicrobial compound disclosed in the reference, 1-ethyl-6,8-difluoro-1,4-dihydro-7-(3-methyl-1-piperazinyl)-4-oxoquinoline-3-carboxylic acid (hereinafter referred to as Compound I).



Gatifloxacin



Compound I

The Examiner takes the position that Applicants' invention possesses the same structural and functional characteristics of the prior art. Applicants respectfully disagree.

That is, it is quite clear from a comparison of the structural characteristics shown by the formulae set forth above that Gatifloxacin of the present invention does not have the same structural characteristics as Compound I of Ogata et al. Gatifloxacin has a methoxy group in place of the fluorine atom of Compound I; and furthermore, Gatifloxacin has a cyclopropyl group in place of the ethyl group of Compound I. The structure of Gatifloxacin is therefore clearly distinct from, and not suggested by, the structure of Compound I. That is, a claim to Gatifloxacin itself would not be rendered obvious by a prior art disclosure of Compound I; and therefore, an aqueous composition containing Gatifloxacin, and a method of using Gatifloxacin, would not be rendered obvious from an aqueous composition containing Compound I or a method of using Compound I.

The Ogata et al. reference also discloses an aqueous liquid composition comprising Compound I and a polyalcohol or boric acid as an isotonizing agent. Further, as pointed out by the Examiner, the reference discloses use of sodium edetate as a chelating agent (column 2, line 44) and no significant changes in coloring and precipitation of Compound I (column 3, lines 66-65).

However, the reference does not teach or suggest the effect of sodium edetate on prevention of coloring and precipitation of Compound I, much less the effect of sodium edetate on raising corneal permeability and prevention of coloring and precipitation of Gatifloxacin.

It should be noted that the presence or absence of disodium edetate does not influence coloration of an aqueous liquid composition of Compound I and, therefore, sodium edetate disclosed in the reference, which is directed to solve a problem in isotonization, is irrelevant to solve a problem of coloration of Gatifloxacin of the present invention. In fact, as seen from Experiment 1 of the attached Rule 1.132 Declaration of K. Inada, one of the present inventors, the aqueous liquid composition of Compound I is a colorless, clear solution regardless of the presence or absence of disodium edetate.*

Further, as seen from Experiment 2 of the Declaration, although concentrated glycerin, which is a kind of polyalcohol, prevents precipitation of crystals of Compound I, disodium edetate cannot prevent participation of crystals of Compound I. Furthermore, as seen from Experiment 3 of the Declaration, only disodium edetate selectively prevents precipitation of crystals of Gatifloxacin, while the other chelating agents disclosed in the reference, i.e., sodium citrate and condensed sodium phosphate, cannot prevent precipitation of crystals of Gatifloxacin.

These results clearly show that, contrary to Examiner's position that Applicants' invention possesses the same functional characteristics of Ogata et al., the functional characteristics are quite different from each other as between the present invention and the reference. The Declaration is thus responsive to the Examiner's suggestion that it is necessary for Applicants to prove that the claimed aqueous composition is functionally different from the aqueous composition taught by the prior art and to establish any patentable differences.

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* An unexecuted Declaration is submitted herewith. The executed Declaration will be filed in the near future.

Accordingly, in view of the foregoing remarks, it is submitted that the ground of the rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

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